Initial Approval: July 11, 2018
Revised Dates: October 9, 2019

CRITERIA FOR PRIOR AUTHORIZATION

Multiple Sclerosis (MS) Agents

~~**PROVIDER GROUP:** Pharmacy Professional~~
BILLING CODE TYPE For drug coverage and provider type information, see the KMAP Reference Codes webpage.

MANUAL GUIDELINES: ~~All dosage forms of the medications listed in Table 1 below will require prior authorization.~~ Prior authorization will be required for all current and future dose forms available. All medication-specific criteria, including drug-specific indication, age, and dose for each agent is defined in table 1 below.

~~**CRITERIA FOR INITIAL APPROVAL FOR ALL PRODUCTS**~~ **GENERAL CRITERIA FOR INITIAL PRIOR AUTHORIZATION:** (must meet all of the following)

- ~~Patient must have a diagnosis of a relapsing form of multiple sclerosis (MS).~~
  - ~~For Ocrevus – patient must have a diagnosis of relapsing or primary progressive forms of MS (i.e. RRMS or PPMS)~~
- ~~Medication must be prescribed within an FDA-approved age range.~~
- Must be approved for the indication, age, and not exceed dosing limits listed in Table 1. Refer to table 3 for definitions of types of disease.
- Medication must be prescribed by or in consultation with a neurologist.
- ~~Dose and frequency of medication requested must be consistent with FDA-approved labeling.~~
- For all agents listed, the preferred PDL drug, which treats the PA indication, is required unless the patient meets the non-preferred PDL PA criteria.
- Patient must not be on concurrent therapy with another disease modifying MS agent ~~(defined~~ listed in table 2.~~)~~
- ~~Prescriber must attest that all additional medication-specific safety criteria, as defined in table 1, is met.~~

~~**TABLE 1. MEDICATION-SPECIFIC CRITERIA**~~

~~MEDICATION~~	~~AGE (years)~~	~~QUANTITY LIMIT~~	~~MEDICATION-SPECIFIC SAFETY CRITERIA~~
~~Ampyra® (dalfampridine)~~	~~≥18~~	~~2 units/day~~	~~➢ Patient must not have a seizure disorder.~~ ~~➢ Patient must not have renal failure or renal impairment defined as CrCl ≤ 50 mL/min.~~
~~Aubagio® (teriflunomide)~~	~~≥18~~	~~1 unit/day~~	~~➢ Patient must not be taking leflunomide concurrently~~ ~~➢ Female patients must use contraception concurrently with Aubagio and must have a negative pregnancy test within 30 days prior to initiation of therapy~~ ~~➢ Patient must be evaluated for latent tuberculosis (TB) with a TB skin test prior to initial prior authorization approval~~
~~Avonex (interferon beta-1a)~~	~~≥18~~	~~1 kit (4 units)/28 days~~	
~~Betaseron (interferon beta-1b)~~	~~≥18~~	~~1 kit (14 units)/28 days~~	
~~Copaxone® (glatiramer)~~	~~≥18~~	~~1 kit (12 or 30 units)/30 days~~	
~~Extavia (interferon beta-1b~~	~~≥18~~	~~1 kit (15 units)/30 days~~	
~~Gilenya® (fingolimod)~~	~~≥10~~	~~1 unit/day~~	~~➢ Patient must not have any of the following:~~ ~~○ Myocardial infarction in past 6 months, unstable angina, stroke, transient ischemic attack, decompensated heart failure requiring hospitalization, and class III/IV heart failure~~ ~~○ Morbitz Type II 2nd degree or 3rd degree AV block or sick sinus syndrome (unless a pacemaker is being used)~~ ~~○ Baseline QTC interval ≥ 500 ms~~ ~~○ Concurrent therapy will Class Ia or Class III antiarrhythmic medications in the past 45 days~~ ~~➢ Patient must not be John Cunningham Virus (JCV) positive~~

~~Table 1 (cont.). Medication-Specific CriteriaMEDICATION~~	~~AGE (years)~~	~~QUANTITY LIMIT~~	~~MEDICATION-SPECIFIC SAFETY CRITERIA~~
~~Glatopa® (glatiramer)~~	~~≥18~~	~~1 kit (12 or 30 units)/30 days~~	
~~Lemtrada® (alemtuzumab)~~	~~≥17~~	~~60 mg total 1st cycle; 36 mg total 2nd cycle (1 year later)~~	~~➢ Patient must have had an inadequate response to two or more drugs indicated for the treatment of MS~~ ~~➢ Patient must not have human immunodeficiency virus (HIV)~~ ~~➢ Patient must have the following lab test completed prior to initial approval:~~ ~~○ CBC, serum creatinine level, urinalysis with urine cell counts, thyroid function~~
~~Ocrevus™ (ocrelizumab)~~	~~≥18~~	~~300 mg day 1, 300 mg 2 weeks later, 600 mg every 6 months~~	~~➢ Patient must not have active hepatitis B virus (HBV), confirmed by positive results for HBsAg and anti-HBV tests~~ ~~➢ –~~
~~Plegridy (interferon beta-1a)~~	~~≥18~~	~~1 kit (2 units)/28 days~~	
~~Rebif (interferon beta-1a)~~	~~≥18~~	~~1 kit (12 units)/28 days~~	
~~Tecfidera® (dimethyl fumarate)~~	~~≥18~~	~~2 units/day~~	~~➢ Prescriber must monitor CBC with differential at baseline and every 6 months (or earlier if clinically indicated).~~ ~~○ Absolute lymphocyte count should not be <500~~
~~Tysabri® (natalizumab)~~	~~≥18~~	~~300 mg/28 days~~	~~➢ Patient, prescriber and infusion center must be registered with the MS Touch Program~~ ~~➢ –~~ ~~*For a diagnosis of Crohn's disease, please see the Immunomodulators criteria~~

Table 1. FDA-approved age and dosing limits for Multiple Sclerosis (MS) Agents[3-17]

Agents	Indication(s)	Age	Dosing Limits
Anti-CD20 Monoclonal Antibodies			
Ocrelizumab (Ocrevus™)	PPMS, CIS, RRMS, SPMS	≥ 18 years	300 mg IV on day 1, followed by 300 mg IV 2 weeks later, subsequent doses of 600 mg IV are administered once every 6 months (beginning 6 months after the first 300 mg dose)
Anti-CD52 Monoclonal Antibodies			
Alemtuzumab (Lemtrada®)	RRMS	≥ 18 years	12 mg/day IV on 5 consecutive days (total 60 mg) followed 12 months later by 12 mg IV daily for 3 consecutive days (total 36 mg)
Fumaric Acid Derivatives			
Dimethyl Fumarate (Tecfidera®)	CIS, RRMS, SPMS	≥ 18 years	240 mg orally twice daily
Interferons			
Interferon Beta-1a (Avonex®)	CIS, RRMS, SPMS	≥ 18 years	30 mcg IM once per week
Interferon Beta-1a (Rebif®)	CIS, RRMS, SPMS	≥ 18 years	44 mcg SC 3 times per week
Interferon Beta-1b (Betaseron®, Extavia®)	CIS, RRMS, SPMS	≥ 18 years	0.25 mg SC every other day
Peginterferon Beta-1a (Plegridy®)	CIS, RRMS, SPMS	≥ 18 years	63 mcg SC on day 1, 94 mcg SC on day 15, then 125 mcg SC on day 29 and every 14 days thereafter
Miscellaneous Biologic Immunosuppressants			
Glatiramer (Copaxone®)	CIS, RRMS, SPMS	≥ 18 years	Multiple sclerosis, relapsing: 20 mg SC once daily or 40 mg SC 3 times per week

Glatiramer (Glatopa®)	CIS, RRMS, SPMS	≥ 18 years	Multiple sclerosis, relapsing: 20 mg SC once daily
Purine Analog Antimetabolites			
Cladribine (Mavenclad®)	RRMS, SPMS	≥ 18 years	3.5 mg/kg orally over a 2-year treatment course, administered as 1.75 mg/kg in each year, no more than 20 mg per day
Pyrimidine Synthesis Inhibitors			
Teriflunomide (Aubagio®)	CIS, RRMS, SPMS	≥ 18 years	14 mg orally once daily
Selective Adhesion-Molecule Inhibitors			
Natalizumab (Tysabri®)	CIS, RRMS, SPMS	≥ 18 years	300 mg IV infusion every 4 weeks
Sphingosine 1-Phosphate (S1P) Receptor Modulator			
Fingolimod (Gilenya®)	CIS, RRMS, SPMS	≥ 10 years	Adults: 0.5 mg orally once daily Pediatric: ≥10 years of age and ≤40 kg: 0.25 mg orally once daily ≥10 years of age and >40 kg: 0.5 mg orally once daily
Siponimod (Mayzent®)	CIS, RRMS, SPMS	≥ 18 years	CYP2C9 Genotype *1/*1, *1/*2, or *2/*2: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1.25 mg once daily on Day 5, then 2 mg once daily, beginning on Day 6 CYP2C9 Genotype *1/*3 or *2/*3: 0.25 mg orally once daily on Days 1 and 2, then 0.5 mg once daily on Day 3, then 0.75 mg once daily on Day 4, then 1 mg once daily, beginning on Day 5

IV: intravenously. SC: subcutaneously. IM: intramuscularly. CIS: clinically isolated syndrome.
RRMS: relapsing-remitting multiple sclerosis. SPMS: secondary progressive multiple sclerosis.
PPMS: primary progressive multiple sclerosis.

LENGTH OF APPROVAL: 12 months

~~**CRITERIA FOR RENEWAL FOR ALL PRODUCTS**~~ **CRITERIA FOR RENEWAL PRIOR AUTHORIZATION:** (must meet ~~one~~ all of the following)

- Prescriber must attest that the patient has received clinical benefit from continuous treatment with the requested medication.[2]
- ~~Prescriber must attest that all additional medication-specific safety criteria, as defined in table 1, is met.~~
- Must not exceed dosing limits listed in Table 1.
- For Lemtrada (alemtuzumab): therapy does not exceed 2 total treatments (5 consecutive days of injections in the first year and 3 consecutive days of injections in the second year)

LENGTH OF APPROVAL: 12 months

DRAFT PA Criteria

FOR DRUGS THAT HAVE A CURRENT PA REQUIREMENT, BUT NOT FOR THE NEWLY APPROVED INDICATIONS, FOR OTHER FDA-APPROVED INDICATIONS, AND FOR CHANGES TO AGE REQUIREMENTS NOT LISTED WITHIN THE PA CRITERIA:

- **THE PA REQUEST WILL BE REVIEWED BASED UPON THE FOLLOWING PACKAGE INSERT INFORMATION: INDICATION, AGE, DOSE, AND ANY PRE-REQUISITE TREATMENT REQUIREMENTS FOR THAT INDICATION.**

LENGTH OF APPROVAL (INITIAL AND RENEWAL): 12 months

Table 2. List of disease--modifying ~~agents~~ therapies (DMTAs) (agents not to be used concurrently)

Disease--Modifying ~~Agents~~ Therapies (~~DMAs~~DMTs)		
~~Ampyra® (dalfampridine)~~ Aubagio® (teriflunomide)	Gilenya® (fingolimod)	Plegridy (interferon beta-1a)
Avonex (interferon beta-1a)	Glatopa® (glatiramer)	Rebif (interferon beta-1a)
Betaseron (interferon beta-1b)	Mitoxantrone	Tecfidera® (dimethyl fumarate)
Copaxone® (glatiramer)	Lemtrada® (alemtuzumab)	Tysabri® (natalizumab)
Extavia (interferon beta-1b	Ocrevus™ (ocrelizumab)	

~~**TABLE 3. COVERED PROVIDER GROUP**~~

~~**PROVIDER GROUP**~~	~~**MEDICATION**~~
~~Pharmacy~~	~~Ampyra, Aubagio, Avonex, Betaseron, Copaxone, Extavia, Gilenya, Glatopa, Plegridy, Rebif, Tecfidera~~
~~Professional~~	~~Avonex, Betaseron, Copaxone, Extavia, Glatopa, Lemtrada, Ocrevus, Plegridy, Rebif Tysabri,~~

Table 3: Definitions of types of MS[1]

Clinically Isolated Syndrome (CIS)	First clinical episode that is suggestive of MS. no evidence of previous episodes of demyelination from the patient's history.
Relapsing-remitting MS (RRMS)	Clearly defined attacks (also known as relapses or exacerbations) with full or incomplete recovery. There is minimal disease progression during the periods between disease relapses, at least as traditionally understood, though relapses themselves may leave severe residual disability.
Active secondary progressive MS (SPMS)	An initial relapsing-remitting MS disease course followed by gradual worsening with or without occasional relapses, minor remissions, and plateaus. The transition from relapsing-remitting MS to secondary progressive MS usually occurs 10 to 20 years after disease onset. Active disease is characterized with relapses and/or evidence of new MRI activity.
Primary progressive MS (PPMS)	Relatively steady progression of symptoms over time. Progressive accumulation of disability from disease onset with occasional plateaus, temporary minor improvements, or acute relapses still consistent with the definition. The most common clinical presentation is a spinal cord syndrome that worsens over months or years with asymmetric spastic paraparesis and no clear sensory level.

Notes:

Lemtrada (alemtuzumab)	Generally reserved for patients who have had an inadequate response to 2 or more medications indicated for the treatment of MS. Subsequent treatment courses of 12 mg IV daily for 3 consecutive days (total 36 mg) may be administered if necessary; courses should be administered no earlier than 12 months after the last dose of the prior treatment cycle.
Mavenclad (cladribine)	Dosing is 3.5 mg/kg over 2-year treatment course, administered as 1.75 mg/kg in each year. Divide the 1.75 mg/kg dose over 2 cycles, each cycle lasting 4 to 5 consecutive days. In the first-year treatment course, initiate the first cycle at any time; administer the

	second cycle 23 to 27 days after the last dose of the first cycle. In the second-year treatment course, initiate the first cycle ≥43 weeks after the last dose of the first year's second cycle. Administer the second cycle 23 to 27 days after the last dose of the second year's first cycle. Following 2 years of treatment, do not administer oral cladribine during the next 2 years. Maximum dose:3.5 mg/kg over 2 years; 20 mg/day.
Zinbryta (daclizumab)	Voluntarily withdrawn from the market in 2018.

References

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3. Ocrevus (ocrelizumab) [prescribing information]. South San Francisco, CA: Genetech Inc; July 2019.
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6. Avonex (interferon beta-1a) [prescribing information]. Cambridge, MA: Biogen Idec Inc; July 2019.
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8. Betaseron (interferon beta-1b) [prescribing information]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; April 2016.
9. Extavia (interferon beta-1b) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2018.
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13. Mavenclad (cladribine tablets) [prescribing information]. Rockland, MA: EMD Serono Inc; April 2019.
14. Aubagio (teriflunomide) [prescribing information]. Cambridge, MA: Genzyme Corporation; July 2019.
15. Tysabri (natalizumab) [prescribing information]. Cambridge, MA: Biogen Inc; Aug 2019.
16. Gilenya (fingolimod) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2019.
17. Mayzent (siponimod) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2019.

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DRUG UTILIZATION REVIEW COMMITTEE CHAIR

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DATE

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PHARMACY PROGRAM MANAGER
DIVISION OF HEALTH CARE FINANCE
KANSAS DEPARTMENT OF HEALTH AND ENVIRONMENT

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DATE